

## Multiple Sclerosis: An Unsolved Problem

THE PUZZLE OF MULTIPLE SCLEROSIS has attracted the attention of investigators in the field of neurology for many years. Etiological theories have been offered in plethora in the past, and even in the last twenty years widely different causes have been suggested, including spirochetal infection,<sup>1,2</sup> non-immune lipolytic agents,<sup>3</sup> and vascular disturbance secondary to increased platelet stickiness.<sup>4</sup> None of these theories is given serious credence at present, but their sheer diversity reflects the continuing uncertainty about the roots of the disorder.

Although the cause of multiple sclerosis is still unknown, the view most favored currently is that the disease is immunologically mediated and further that a remote early-life exposure, perhaps a viral infection, may be the original event. Most of the evidence to support this notion comes from two lines of research: (1) epidemiological studies, and (2) investigations of experimental allergic encephalomyelitis (EAE) in animals. The epidemiological evidence is at best indirect, and the validity of the findings in EAE depends upon how faithfully EAE represents a model of multiple sclerosis, a point which deserves further comment. Elsewhere in this issue of CALIFORNIA MEDICINE, Seil has set forth in satisfying detail the experimental evidence, particularly that gained from the study of EAE, which has served to shape current opinion.

EAE is an acute monophasic illness from which the animal either dies or recovers completely. Neither clinically nor pathologically does EAE resemble chronic multiple sclerosis, and a chronic fluctuating form of EAE analogous to multiple sclerosis has not been produced experimentally.

Why, then, has EAE been studied so extensively? The major reasons are, as summarized by Alvord,<sup>5</sup> (1) the finding of serum antibodies in both EAE and active multiple sclerosis which will demyelinate central nervous system tissue cultures, (2) the close resemblance pathologically of multiple sclerosis to the cerebral form of rabies post vaccinal encephalomyelitis, which is considered to be human EAE, and (3) the remarkably similar susceptibility, according to age group, to multiple sclerosis and to rabies post-vaccinal encephalomyelitis. These observations form the link between multiple sclerosis and EAE.

Claims of successful treatments for multiple sclerosis have been even more variegated and fanciful than theories as to its cause. Partly this is due to the variable and remittent nature of the illness, which on occasion permits any therapeutic measure to appear effective. In view of the intense research interest in the immunological aspects of multiple sclerosis, one would expect that immuno-suppressive agents other than corticosteroids and ACTH are under investigation. To date, only a few uncontrolled pilot studies have been reported, and no large-scale, controlled program has been undertaken. At present the only generally accepted method of therapy is short-term, high dosage adrenocorticotrophic hormone for recent worsening of the disease.<sup>6</sup> There is an equally good rationale for using dexamethasone instead of ACTH, but so far only ACTH has been subjected to a large systematic study.

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